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Viruses and Life: Can There Be One Without the Other?

Matti Jalasvuori, Ph.D., and Jaana K.H. Bamford, Ph.D.,
Department of Biological and Environmental Science and Nanoscience Center, University of Jyväskylä, P.O. Box 35, 40014 University of Jyväskylä, Finland.

Abstract

Viruses are omnipresent, genetically replicating parasites in our biosphere that affect and drive the evolution of life in various ways. Are viruses an inevitable feature of all naturally emerged (although hypothetical) living systems in the Universe or are they only a specialty of our life on Earth? We argue in this discussion that viruses indeed might be present in extraterrestrial, independently emerged biospheres, at least if the process of the origin of life was similar to that on Earth. Viruses are likely to have played important roles in the evolution of early life and thus their presence or absence could dictate the direction of the evolution of life in all living systems.

Keywords: Origin of viruses, extraterrestrial life, origin of life, hydrothermal vents, virus evolution

1. INTRODUCTION

For what parts would a potential life elsewhere in the universe resemble the life on Earth? This is the question that is often asked when certain characteristics appear to be uniform for the life on our planet. Does alien life use DNA as their genetic material as all known cellular organisms do? Or is it perhaps only the principle of base-pairing that any independently emerged life might use for guiding the replication and synthesis of genetic progeny? Evolutionary principles, for one, would inevitably guide the selection of genetically replicating agents anywhere in the universe (Joseph and Schild 2010). What about viruses? They are obligatory cellular parasites that have their own genome enclosed into a protective protein shell (known as a capsid). Viruses are very abundant on Earth, outstripping the number of their host cells by a tenfold (Bergh et al. 1989). All cellular life forms are thus constantly under a siege of a viral armada and this everlasting battle for survival has been argued to have played a major role in the evolution of life

(Joseph 2009; Villarreal, 2005). Should we expect to find viruses from other extraterrestrial ecosystems? Are viruses such an essential feature of life that you cannot have an ecosystem without them? We argue here that this might indeed be the case.

2. EARLY ORIGIN OF VIRUSES

If we are asking whether there would be viruses infecting cellular life elsewhere in the universe, we need to understand how viruses emerged here on Earth. However, there is no consensus among scientists for explaining the origin of viruses, but there are some lucrative evidence pointing towards the very early origin of viruses.

Certain bacterial, eukaryal and archaeal viruses share many common characteristics. The so-called double beta-barrel containing capsid protein lineage consists of icosahedral viruses that (usually) have an inner membrane beneath the protein capsid (Krupovic and Bamford, 2008a). In these viruses the capsid itself is formed of a unique type of a protein, which is folded into a double-beta barrel conformation. Moreover, the machinery by which these viruses package their genome into the capsid is shared by most of these viruses (Strömsten et al. 2005). Bacterial virus PRD1 and a human infecting adenovirus were the first ones to be noted to encode double beta-barrel major capsid proteins (Benson et al. 1999). These viruses also utilize similar capsid architecture and have similar proteins for building the base of the vertices in the icosahedron. Later on, other eukaryal viruses infecting various organisms (ranging from algae to fish) were designated to belong to the same structural virus lineage (Abrescia et al. 2004). Eventually the lineage was expanded to *Crenarchaea* by the demonstration that an inner membrane containing Sulfolobus Turreted Icosahedral Virus (STIV) encoded a double beta-barrel protein (Khayat et al. 2005). There are STIV-related integrated viruses also in *Euryarchaeal* chromosomes (Krupovic & Bamford, 2008b). Nevertheless, these types of viruses appeared to infect cellular organisms situated at various points in the tree of life. The common features of the double betabarrel lineage is most plausibly explained by a scenario, in which the common ancestor of these viruses existed already before the last universal common (cellular) ancestor (LUCA), and this virus then diverged to evolve along with its independent hosts organisms (Krupovic and Bamford, 2008a).

The double beta-barrel lineage, however, is not the only group of viruses that is most likely to be of ancient origin. After the discovery of the first ancient viral group, several more have been identified.

The very abundant bacterial viruses with a head to tail morphology appear to be related by their capsid architecture to several archaeal viruses and to (human) herpes viruses (Baker et al. 2005; Akita et al. 2008). Furthermore, the RNA genome containing reovirus-like viruses that infect both bacteria and eukaryotes are most likely related to each other (Bamford et al. 2005). Recently the

pleomorphic archaeal and bacterial viruses were suggested to be evolutionarily related (Pietilä et al. 2009).

Evolutionary comparisons of all of these viral lineages suggest that their respective common ancestors might have existed very long time ago, perhaps before the LUCA. The very diverse crenarchaeal viruses that have been isolated from geothermally heated environments can also be of an early origin (Ortmann et al. 2006; Prangishvili et al. 2006). Their diversity might only reflect the better survival ratio of their hyperthermophilic hosts during massive meteorite or comet impact events that have drastically elevated the surface temperature of our planet (Jalasvuori and Bamford, 2009) especially during the period of accretion during the first 700 million years.

The early origin of viruses is also supported by our recent demonstration that the inner-membrane containing viruses infecting thermophilic bacteria and halophilic archaea appear to be most closely related to each other, but more distantly related to the double beta-barrel viruses (Jalasvuori et al. 2009; Jalasvuori et al. 2010a). The major capsid protein of these viruses appears to be a single beta-barrel, which others and we have argued to be the evolutionary precursor of the double beta-barrel capsid protein. In other words, the double beta-barrel and the single beta-barrel capsid viruses share a common icosahedral morphology, an inner membrane and a similar genome packaging apparatus, and therefore it is likely that these two ancient lineages of viruses also share a common ancestor. Probably the ancestor diverged into two different lineages already before *Bacteria* and *Archaea* separated into the two distinct domains of life.

Altogether, the evidence suggests that the very abundant world of viruses appear to be formed of lineages that emerged before the first cellular domain of life emerged (Benson et al. 2004). It has been suggested that viruses could be of extraterrestrial origin (Joseph and Schild, 2010; Joseph and Wickramasinghe 2010), thus potentially explaining their deep phylogenetic connections with cellular life. However, we argue that it is more likely that the evolutionary process producing both cells and viruses were actually tightly associated to one another. Was the origin of these several viral lineages an inevitable consequence of events that occurred in the primordial hatchery of life?

3. WHAT ROLE MIGHT VIRUSES HAVE PLAYED IN THE EVOLUTION OF PRIMORDIAL LIFE?

What could explain the early emergence of capsid containing parasites? Parasitism itself appears to be common to any process that can be parasitized. Therefore it is likely that viral parasites emerged as soon as parasitism was possible to be maintained within the very early, cell-like entities. However, during the first steps of life, the proto-viruses (along with their capsid encoding potential) might not

have been parasites in the usual sense but instead an essential part of the early community of life.

Life on Earth emerged about four billion years ago (Battistuzzi et al. 2004; Nemchin et al. 2008; O'Neil et al. 2008). The very first life forms must have been something relatively simple. Competition, selection and genetic innovations eventually increased the complexity of the primitive life. Alkaline, warm hydrothermal vents with bubble-like micro-compartments have been suggested to serve as an ideal alternative to the earlier "primordial soup: hypothesis for the location of origin of life (Milner-White and Russell 2010; Nitschke and Russell 2010; Russell and Kanik 2010; Russell et al. 1994). Compartmentalization has been argued to be essential to early life because it helped the emerging life to maintain the integrity of molecular systems that associated with metabolism and allowed different systems to vary in their compositions (Monnard and Deamer, 2002). Koonin and Martin refined the previously presented idea that life emerged on submarine hydrothermal vents (Koonin and Martin, 2005). Their scenario suggested that life originated in a warm geothermally heated vent within a system of contiguous iron-sulfide compartments where primitive virus-like RNA molecules, perhaps encoding some proteins, emerged and begun to evolve. The first "cells" were not free-living independent organisms but instead a compartment-dependent communities of replicators and other agents. Martin and Russell have suggested that the basic biochemistry was first to emerge in these alkaline vents and only later the genetic replicators appeared to the scene (Martin and Russell, 2007; Milner-White and Russell 2010; Nitschke and Russell 2010; Russell and Kanik 2010). Nevertheless, some sort of biological replicators had to emerge eventually and thus kick-start the Darwinian evolution of life.

What role could the early viruses have played in such a primordial ecosystem? Carl Woese has argued that before the origin of major cellular domains the early life evolved mainly horizontally rather than vertically (Woese, 2000; Woese, 2002). In other words, the emerging life-forms readily exchanged genetic information between primordial cell-structures. Koonin et al. (2006) suggested that viruses must be of early origin and the role of viruses in the early evolution of life was important. In order to support the early origin of viruses they argued that several genes coding for viral replication and morphogenesis and for capsid formation are shared by several viruses but are missing from cellular life forms. In their concept, the primary lineages of viruses and related selfish agents emerged from the primordial pool of primitive genetic elements. The RNA viruses were the first to evolve, and were followed by retroid elements (corresponding to the RNA to DNA transition as genetic material) and eventually DNA viruses. The viruses emerged much before the true cells and thus the early viruses allowed extensive gene mixing within the emerging living system in the primordial world. They suggested that virus-genes that formed during the first steps of evolution have direct and uninterrupted descendants among many of the modern viruses.

In 1994 Koch argued that there is no trivial spontaneous way for polynucleotides to be introduced into living cells and thus transfer of genes from one "organism" to another did not occur among the primordial life forms. However, we argue that viruses are exactly something that transfers polynucleotides from one cell to another. Thus, even if genes cannot be spontaneously introduced to emerging cells, there might have been primordial, genetically encoded agents making the genetic transfer possible. Vetsigian et al. (2008) argued that the universal genetic code was an innovation sharing protocol between early life forms. Natural selection would have favored the system to maintain a single decoding alphabet for genes (Joseph and Schild 2010). Following this line of reasoning, we suggested that the emerging viruses could have played an important role in sharing innovations between the compartments where life might have originated (Jalasvuori and Bamford, 2008). In our model any capsid-encoding genes could have been evolutionarily favored within a primitive community of membrane enclosed protocells due to their potential for transferring beneficial genetic innovations from one proto-cell to another. Along with the innovations, they might have spread their "viral" genes and thus further amplifying the process of genetic exchange between cells. In 2005 Lehto and Karetnikov argued that the present-day RNA-viruses and viroids could resemble for some parts the early replicators in their molecular and functional attributes. Indeed, we showed that within a simulated compartment-matrix (inhabited by ribozyme-like agents) virus-like capsid-encoding genes are favored due to their ability to transfer genetic innovations between proto-cells (Jalasvuori et al. 2010b). We compared the rates by which the systems evolved to the predefined maximum of genes. In the presence of capsid-like genes the systems reached the maximum gene-capacity faster than in the absence of these genes. This suggests that systems containing capsid-like genes would possibly outcompete non-capsid systems. However, the simulated proto-cells had to come up with innovations that helped them to combat parasites in order for the innovation sharing to be beneficial as in absence of the defense mechanisms the capsid-like genes would only spread the destructive parasites instead of beneficial innovations.

Nevertheless, during the evolution of the primordial community, many genetic innovations could have accumulated into the proto-cells and thus the cells may have less relied on extracellular resources (like e.g. the abiotically formed amino acids) for the purposes of replicating and producing cellular components. It is possible that some of the virus-like entities turned into pure resource consuming parasites (like modern viruses), because these parasitic phenotypes were able to outcompete the "beneficial" innovation-sharing viruses in terms of reproductive success (Jalasvuori and Bamford, 2008). This might have caused the proto-cells to favor any trait that isolated them from the community since isolation probably helped to avoid virus infections. Emerging cell walls, for example, could have reduced the possibility of virus-parasites to enter the proto-cell. We have recently demonstrated that viruses (exploiting the sex apparatuses of prokaryotic cells) effectively removed the ability of bacteria to horizontally exchange genetic material with one another (unpublished results). Therefore it seems plausible to

expect similar evolution to have occurred in primordial entities. In other words, if the easily intruded proto-cells became invaded and killed off by viral parasites, we should expect the hard-to- invade proto-cells to prevail. Eventually the population of proto-cells would encompass mostly of the hard-to-invade cells. However, viruses would also evolve and invade the more isolated cells and thus the cycle to favor even more isolated or otherwise virus-resistant cells would be repeated. It is possible that due to viral selection, the system would at some point be comprised of cells that are very consistent packages of genes with as little as possible (genetic) exchange with other cells.

We may consider immunocompromised patients as a rough analog: they are not able to defend themselves against viral infections and thus they fail to survive in the world of viruses. If there were no pathogens, then immunodeficiency would be a less fatal condition. In other words, some sort of an immune system had to evolve for complex life to survive in the world of microbes. Did the independency of the first bacterial and archaeal cells evolve similarly in response to the viral selection?

On the other hand, we may consider the obligate intracellular parasites, such as *Rickettsia* (Andersson et al. 1998), as an analog of proto-cells that are incapable of surviving on their own. They rely on the external resources, such as the host's amino acids, to such as extent that they are unable to reproduce outside of the host cell. Similarly, if the proto-cells were dependent on the primordial hatchery of life, then they could not have left the hatchery. If there was a virus that would infect *Rickettsia* cells by recognizing, for example, membrane-bound ATP/ADP translocases (a protein by which the parasite introduces the host generated ATP into the cell), then, under viral selection, *Rickettsia* should evolve a greater capacity for generating ATP or otherwise become virus resistant. There are indeed bacterial viruses of endosymbiotic bacteria of *Rickettsiales* (Kent & Bordenstein, 2010) and thus there is a possibility that this hypothesis could be experimentally tested.

It is also possible that viruses played a role in the emergence of the endomembrane system in protoeukaryotes. This discussion merely plays with very hypothetical ideas. However, since the current knowledge on eukaryogenesis is far from being conclusive, then such discussions might help promoting the formulation of more plausible models. Nevertheless, eukaryotes present the most complex cell-type on Earth and arguably complex organisms would never have emerged if eukaryotes had never evolved. From this point of view it would be interesting to try understanding whether viruses had a role in origin of eukaryotes (as has been argued, see e.g. Villarreal, 2005; Joseph 2010).

What is known about eukaryal endomembrane system? Membrane bound organs, such as nucleus, Golgi apparatus, endoplasmic reticulum and mitochondria compartmentalize eukaryotic cells. The organs reside in the cytosol as somewhat independent components. The operation of the membrane bound compartments

involves constant vesicle fusions and buddings, as there is continuous back and forth traffic of vesicles between the cell surface and various organs. Primitive eukaryotes already had complex endomembranes (Dacks and Field, 2007) and all modern eukaryotes have evolved from a mitochondria-bearing ancestor (Embley and Martin, 2006; Embley et al. 2003). The ancestor of modern mithochondria was a bacterium, related to Rickettsia (see above; Andersson et al. 1998), that established a symbiotic relationship with the very first eukaryotes. Moreover, some (but not all) eukaryal genes are related to archaeal and bacterial organisms (Koonin, 2006; Hartman & Fedorov, 2002; Rivera & Lake, 2004; Horiike et al. 2001; Podar et al. 2008; Yutin et al. 2008).

Viruses were also proposed to have played a role in the origin of nucleus and other eukaryal features (Bell, 2001; Forterre, 2006; Takemura, 2001; Villareal, 2005; Villarreal & DeFilippis, 2000; Koonin et al. 2006). For example, certain viruses have linear, eukaryote-like genomes and they replicate their DNA in a similar manner. Some viruses possess eukaryote specific DNA-repairing enzymes. Many viruses have features with functional similarities to nuclear pores and some viruses extrude messenger RNAs from the virion in a somewhat similar way with the nucleus. Furthermore, there are some putative simple endomembrane homologues in prokaryotes (Dacks and Field, 2007). Bacteria of the *Planctomucetes* genus have a membrane-enclosed nucleoid (Fuerst, 2005), and in the archaeon *Ignicoccus islandicus* small vesicles can be observed in electron microscope micrographs (Rachel et al. 2002). Components representative of ER translocational system of eukaryotes is also present in prokaryotic SRP/SecY translocation system (Gribaldo and Cammarano, 1998) and bacterial dynaminlike protein (among some other features) has been described (Low and Lowe, 2006). Yet, most features of any resemblance to inner lipid compartments of eukaryotes appear to be absent in the currently studied prokaryotes. Could some of their encoding genes be found from the very diverse viral genomes?

The last common eukaryote ancestor already possessed endomembrane system of high complexity and this system was suggested to have formed autogenously from pre-existing building blocks of domains and motifs (Dacks and Field, 2007). Indeed, endoplasmic reticulum, nuclear envelope, sophisticated transporting machinery, Golgi-apparatus and dedicated vesicles are novel evolutionary steps in cellular development. Did some of the domains and motifs emerge in the genomes virus-like parasites? Viruses must have been manipulating the entry and exit through cellular membrane much before the emergence of modern eukaryotes (Joseph 2010) and thus they probably encoded some suitable proteins for facilitating the vesicle-traffic. Perhaps the proto-eukaryotes inhabited a compartment-community somewhat similar to that in which life might have emerged. Within this system virus-like entities could have played similar roles during the emergence of life and thus some of the viruses could have had the chance to establish a symbiotic relationship with a cell and thus provide the core for an evolving nucleus. Some of the other parts of the machinery behind

endomembrane system could similarly be of viral, but also of bacterial and archaeal origin as all these entities might have inhabited the same environment with proto-eukaryotes (Joseph 2010).

Most of the current debate addressing the origin of eukaryotes revolves around the question whether it was an archaeon and a bacterium that fused to produce the eukaryote or if it was some form of protoeukaryote and bacterium that formed the eukaryal cell. Perhaps the genetic evidence alone is not enough to provide a sufficient model for explaining why eukaryotic cells formed. We should also consider the contribution of the potential habitat of the proto-eukaryotes in the evolution towards the modern eukaryotic cell. In any case, being relevant or not, the origin of eukaryotes had to occur *somewhere* and all life forms on Earth are adapted to live in their particular *somewhere* (with the other inhabitants of the same environment). Were the gradual adaptations in emerging eukaryotes only favorable in this specific environment? No intermediates between the prokaryotic and eukaryotic cells have been discovered. Therefore, it is possible that eukaryotes emerged as compartment-dependent entities in a protected community and thus the first, free-living, non-compartment-dependent eukaryotes were already fully formed organisms. This process should not have left any free-living intermediates of eukaryogenesis to be discovered.

4. CONCLUSION

Viruses could have been important actors in the stem of life. In the universal scale, virus-like entities might provide a way for any emerging living systems to utilize successful innovations as a community rather than forcing the proto-cells or other primitive structures to evolve alone (Joseph 2010). Spontaneous origin of life might require tiny compartments where necessary compounds for the emerging replicators concentrate. That life elsewhere in the Universe might have originated within such environments and thus viruses could be present there as remnants of the natural side- product of the early evolution of the biosphere (Joseph and Schild 2010). Later on in the evolution of primordial life on Earth, viruses might have promoted the isolation of the proto-cells from the community as non-isolated cells could have been easily exploited by viral parasites. Therefore viruses may have been the driving force in the evolution of free-living cellular beings on Earth.

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